

Successful Endoscopic Treatment for High-grade Cervical Intraepithelial Neoplasia with Gross Lesions of the Vagina

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Abstract

We present a patient diagnosed with high-grade cervical intraepithelial neoplasia (CIN) combined with macroscopic lesions of the vaginal epithelium. There was no lesion in pelvic magnetic resonance imaging examination, and histopathological examination revealed CIN3 and vaginal intraepithelial neoplasia (VAIN) 3 without invasion. We chose minimally invasive surgery for her and total laparoscopic hysterectomy with partial resection of the vagina was carried out. To determine appropriate surgical margins, vaginal colpotomy was performed. No recurrence of VAIN has been observed to date that passed for 9 months either.

Keywords: Cervical intraepithelial neoplasia, laparoscopy, vaginal intraepithelial neoplasia

INTRODUCTION

Cervical intraepithelial neoplasia (CIN), especially high-grade CIN, is the clinical precursor to cervical squamous cell carcinoma. Without appropriate treatment, progression to invasive carcinoma is estimated to occur in 20% of patients.^[1] Stage I B cervical carcinoma by the International Federation of Gynecology and Obstetrics staging is defined as clinical lesions confined to the cervix. All gross lesions, even with superficial invasion, are Stage I B carcinomas. We report a woman diagnosed with a high-grade squamous intraepithelial lesion (HSIL)/CIN3 without stromal involvement despite the presence of macroscopic white lesions involving the vaginal fornix. The patient underwent total laparoscopic hysterectomy (TLH) and 9 months has passed without recurrence.

CASE REPORT

This patient was a 47-year-old non-gravida woman who had panic disorder for which she took no medication.

Her medical history was otherwise significant for asthma. Abnormal cervical cytology was identified at a routine medical examination, for which she was seen at a nearby general hospital. Cervical biopsy showed carcinoma *in situ* despite macroscopically acetowhite lesions spreading over the uterine cervix and vaginal wall, which were suspected to be invasive carcinoma. Consequently, she was admitted to our hospital to receive a comprehensive examination. Human papillomavirus (HPV) genotype 16 was detected at the previous hospital. We performed colposcopic examination, and after the application of acetic acid, dense leukoplakia was seen in the uterine cervix [Figure 1a]. Furthermore, the lesion extended to the left side of the uterine fornix and vaginal wall. The thick acetowhite lesion with punctation is shown in Figure 1b. Vaginal lesions were continuously expanded from the uterine fornix to the vaginal wall but limited to the upper one-third of the vagina. The histopathological diagnoses were HSIL/CIN3 and vaginal intraepithelial neoplasia 3 (VAIN3).

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Invasive carcinoma was not found. Laboratory evaluation showed the following results: complete blood count and serum chemistry normal; squamous cell carcinoma antigen, 2.0 ng/ml (reference range <1.5 ng/ml); carcinoembryonic antigen, 1.3 ng/ml (reference range <5.0 ng/ml); cancer antigen (CA) 19–9, 20.5 U/ml (reference range <37.0 U/ml); and CA 125, 5.6 U/ml (reference range <35.0 U/ml). Pelvic magnetic resonance imaging showed no lesions in the cervix or vagina [Figure 1c]. In 18F-fluorodeoxyglucose positron-emission tomography/computed tomography, there was no region of specific uptake as would be expected in invasive carcinoma and there was no accumulation suggestive of distant metastasis or lymph node metastasis. Diagnostic conization under spinal anesthesia was performed. During the procedure, a Lugol's iodine negative area was observed in the vaginal wall; the cervical lesion was also negative. Conization and the biopsy of the vaginal lesion were performed using a YAG laser. Histopathological examination of the resected cervical specimen showed severely atypical cells in all layers of the epithelium, but stromal or glandular involvement was not detected. VAIN3 was observed in the vaginal biopsy specimen. There was no evidence of invasive cervical carcinoma. As a result, we decided to perform radical treatment: TLH combined with resection of the vaginal lesions. The uterus and ovaries were macroscopically normal. Dissection of the pararectal and paravesical spaces was performed; the uterine artery was identified and ligated. The fascial adhesion of the bladder was sufficiently released from the cervix and upper vagina. The ureteral tunnel was identified, and the vesicouterine ligament was incised, avoiding damage to the adventitia and

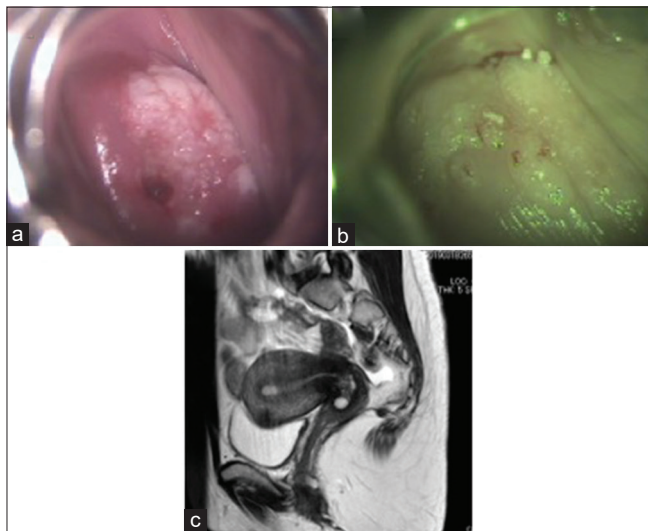


Figure 1: Colposcopic and imaging findings. (a) Colposcopy of the uterine cervix showing acetowhite lesion, (b) colposcopy of the vagina showing the thick acetowhite lesion with punctuation, (c) magnetic resonance imaging of the pelvis (T2-weighted sagittal image) showing no lesions in the cervix or vagina

muscular wall of the ureter, and the ureter was rolled laterally. The rectovaginal septum and the uterosacral ligament were dissected, and the pararectal space was widened. After ligating the paracervical and paravaginal tissues laterally, a transvaginal incision was made to determine an accurate excision line for the vaginal intraepithelial lesion. The operation took 202 min and the blood loss was 100 ml. Histopathological examination revealed overall erosion and partly atypical squamous epithelium; the cell density was high and cells with irregular nuclei were seen around the surface. Invasive carcinoma was not found and the surgical margin was negative [Figure 2]. The final diagnosis was HSIL/CIN3 and VAIN3. The postoperative course was uneventful and she was discharged 5 days after the surgery. Her treatment was complete in accordance with the histopathological examination. Currently, at 9 months after performing surgery, follow-up examinations have not shown any disease recurrence.

DISCUSSION

VAIN is the premalignant stage of vaginal carcinoma and HPV infection is a risk factor for the development of VAIN. CIN also arises due to HPV infection and CIN can exist concurrently with VAIN. However, approximate squamous intraepithelial neoplasia related to HPV infection occurs at the uterine cervix only, and most instances of VAIN are discovered in women who underwent the previous hysterectomy due to cervical squamous neoplasia.^[2,3] In our patient, acetowhite lesions and leukoplakia of the uterine cervix contiguous with a thick acetowhite lesion with punctuation were seen in the vaginal epithelium. CIN3 with extensive VAIN3 is rare, so we considered the possibility of invasive carcinoma. Fortunately, these lesions showed no

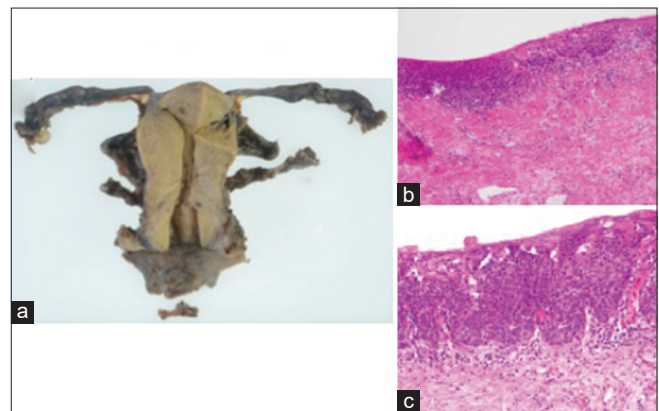


Figure 2: Macroscopic and histopathological findings. (a) Macroscopic view of the formalin-fixed uterus and upper one-third of the vagina, (b) histopathological findings of the cervical epithelium (H and E, ×40), (c) histopathological findings of the vaginal epithelium (H and E, ×200). Full-thickness atypia is found, which manifest as superficial cell nuclear enlargement and koilocytotic atypia, but invasive carcinoma was not found

evidence of invasion, and the area of VAIN3 did not extend halfway down the vaginal wall, enabling us to perform minimally invasive radical surgery.

HPV 16 is the main genotype responsible for high-grade VAIN^[4,5] and HPV16 infection was detected in our patient. The HPV vaccine can prevent HPV-associated diseases such as neoplasia of the female genital tract, as well as carcinomas of the neck, anus, and penis.^[6-9] In Japan, the HPV vaccine is a nationally recommended routine immunization. However, it is not recommended for juvenile women due to some reports of young girls who complained of postvaccination side effects. Most juvenile women have not received the HPV vaccine in recent years and HPV-associated diseases are predicted to increase in Japan. Although CIN and early-stage cervical carcinoma can be treated by conization or trachelectomy for fertility-sparing surgery, fertility-sparing methods are difficult to perform in instances of vaginal neoplasia. Our patient did not wish to preserve fertility, so we were able to perform hysterectomy with partial vaginal resection. If young patients with CIN who have synchronous VAIN hope to preserve fertility, curative therapeutic strategies are limited. Worldwide reduction of HPV-associated anogenital diseases has been reported;^[10] young women who received the HPV vaccine will be protected from HPV infection and can avoid the loss of the genital tract except in Japan. Through this case, we are confident that it is important to realize the early restoration of the HPV vaccine in juvenile women in Japan.

CONCLUSION

We have presented a patient with high-grade CIN and gross lesions of VAIN3. She was treated with minimally invasive surgery with successful resection of the cervical and vaginal neoplasia. CIN and VAIN result from HPV infection, especially HPV genotype 16; the HPV vaccine should adequately prevent these diseases and protect young women from losing fertility.

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Ethical approval and declaration of patient consent

This study was approved by IRB of Hyogo Cancer Center, IRB No. G-105 obtained on November 26, 2019.

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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